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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,194	10/12/2006	Matthew A. Nugent	701586-53702	8409
50607	7590	03/17/2009		
RONALD I. EISENSTEIN 100 SUMMER STREET NIXON PEABODY LLP BOSTON, MA 02110			EXAMINER UNDERDAHL, THANE E	
			ART UNIT	PAPER NUMBER
			1651	
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			03/17/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/552,194	Applicant(s) NUGENT ET AL.	
	Examiner THANE UNDERDAHL	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7-16 and 23-30 is/are pending in the application.
- 4a) Of the above claim(s) 30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-16, 23-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/10/06, 1/4/08, 2/8/08</u> . | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

Response to Restriction/Election

Applicant's response to the species election without traverse filed on 2/21/08 is acknowledged. The applicant elected Group I which includes claims 1-5, 7-16 and 23-30. Upon further review the Examiner recognized that claim 30 is drawn to the method of claim 19 which has been cancelled without traverse. In turn, in the interest of compact prosecution this claim has been withdrawn by the Examiner for being part of a non-elected group. Claims 1-5, 7-16, 23-29 will now be examined on the merits.

Objections to the Claims

Claim 14 is objected to because of the typo "heparin-bind" instead of heparin-binding. Please make appropriate corrections.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 or 103 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Or in the alternative

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5, 7-14, and 23-29 are rejected under 35 U.S.C. 103(a) as obvious over Goerges et al. (Abstract from Annual Meeting of the Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, Available March 20, 2002) in light of

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support by Midwood et al. (Methods in Cell-Matrix Adhesion, 2002) and in light of Miralem et al. (Oncogene (2001) 20, 5511- 5524).

These claims are to a device comprising the following:

- An **extracellular matrix (ECM)** with an internal pH between 4.0 and 6.0,
- This ECM contains either heparin or a heparin related compound such as **heparin sulfate (HS)** or **heparin sulfate proteoglycan (HSPG)** that is bound to a protein.
- This protein has a pH dependant binding to the heparin or heparin related compound

The claims are further limited to the protein being VEGF such as VEGF₁₂₁ or VEGF₁₆₅ that has a heparin-binding consensus sequence that is a glycine-like box as limited in claims 8-11. The claims further limit that the internal pH is between 5 to 6 or about 5.5.

Goerges et al. teach an ECM that contains HSPG that has an increased binding affinity for VEGF₁₆₅ as the pH is decreased. ECM inherently contains fibronectin as supported by Midwood et al. (pg 145). The fibronectin inherently binds to VEGF as supported by Miralem et al. (Figure 2 and page 5521, col 2, top). Thus the ECM of Goerges et al. will inherently comprises fibronectin which will inherently bind VEGF. VEGF₁₆₅ has a heparin-binding consensus sequence with a sequence that matches SEQ ID 1, as well as the sequence limitations of claims 9, 10 and 24-26 (see Applicant's Specification, pg 5).

Claims 13, 27-29 contain product by process limitations that the device must be formed "*in situ* in a subject". Product by Process claims are not limited by the manipulations of the recited steps, only the structure implied by the steps (M.P.E.P. § 2113). As such, these methods of preparation do not impart a functional relationship to the device and are not given patentable weight. Therefore since these claims do not add further structural limitations to the previous claims they are obvious as well.

Claim 14 limits that the composition is a kit that contains:

- heparin or heparin-related compound in a vial
- a second vial containing fibronectin or a protein containing a heparin-binding domain.

The supporting reference by Miralem et al. shows that both heparin and fibronectin are available independently and commercially (pg 5521 col1, middle and col 2, top respectively). Therefore one of ordinary skill in the art would recognize that grouping items that commercially available into a kit is obvious since fibronectin and heparin are used in the same experiments.

Therefore claims 1-5, 7-14, and 23-29 are obvious in view of the above references.

Claims 1-5, 7-15, and 23-29 rejected under 35 U.S.C. 103(a) as being unpatentable over Goerges et al. as applied to claims 1-5, 7-14, and 23-29 above, and further in view of Bell et al. (U.S. Patent # 6179872, January 2001).

While Goerges et al. teach an ECM they do not teach that their ECM is encased in a film, hydrocolloid, hydrogel, foam, gelatin, bead, bondage, and cellophane. Bell et al. teach that ECM can be encased into a biopolymer foam (col 8, lines 25-30). It would be obvious to one of ordinary skill in the art to use the ECM in the invention of Bell et al. since the ECM of Georges et al. this would be a simple matter of substituting one ECM for another (2144.06 II).

Therefore claims 1-5, 7-15, and 23-29 are obvious in view of the above references.

Claims 1-5, 7-14, 16 and 23-29 rejected under 35 U.S.C. 103(a) as being unpatentable over Goerges et al. as applied to claims 1-5, 7-14, and 23-29 above, and further in view of Soker et al. (BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, 1994).

Claim 16 limits the size of the heparin related compound to an oligosaccharide of 8-16 sugars. Goerges et al. does not teach the size of their HSPG. Regardless this would be obvious to one of ordinary skill in the art by the time the invention was made in view of the teachings of Soker et al. They teach that the length of the heparin directly effects the binding activity of VEGF₁₆₅ (Soker, pg 203, Middle of Page). Indeed Soker et al. teach that heparin compounds of 16-18 sugars inhibits binding (Soker, Figure 3A). Therefore it would be obvious to optimize the length of the heparin to ensure the correct binding activity is achieved via routine optimization using Soker et al. as a guide.

Therefore claims 1-5, 7-14, 16 and 23-29 are obvious in view of the above references.

No claims are currently allowed in this application.

In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached Monday through Thursday, 8:00 to 17:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

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published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Thane Underdahl
Art Unit 1651

/Leon B Lankford/
Primary Examiner, Art Unit 1651